Section III. (REMARKS)

Amendment of Specification at Page 13, in Respect of Structural Formula

In Response to the Examiner's noting of a structural informality in the chemical structure set out in the first paragraph on page 13 of the originally filed application, the structural formula has been appropriately set out consistent with the chemical name.

Acknowledgement of Withdrawal of Claims 15 and 17

The Examiner's withdrawal of claims 15 and 17, as drawn to non-elected inventions, is noted.

Submission of Terminal Disclaimer Overcoming Double Patenting Rejection Based on U.S. Patent 6,281,207

In response to the rejection of claims 1-14, 16 and 18-30 on obviousness-type double patenting grounds over claims 1-14 of U.S. Patent No. 6,281,207, a terminal disclaimer is enclosed and submitted herewith, to overcome such rejection.

The fee of $55.00 specified in 37 CFR §1.20(d) for such disclaimer is included in the amount specified in the attached credit card authorization form.. Authorization hereby is given to charge any deficiency in respect of the terminal disclaimer or otherwise in connection with the entry of this response, to Deposit Account Number 08-3284 of Intellectual Property/Technology Law.

Rejection of Claims on Reference Grounds under 35 CFR §102(b) and 35 USC §103(a)

In the July 1, 2003 Office Action, the pending elected claims 1-14, 16, and 18-30 were rejected on various reference grounds:

Claims 1-4, 6-12, 26, 27 and 30 were rejected under 35 USC §102(b) as anticipated by Henry et al., Experimental Neurology (abstract); and

Claims 1-4, 7, 13, 16, 26, and 27 were rejected under 35 USC §102(b) as anticipated by Rawlow et al., European Journal of Pharmacology (abstract); and

Claims 1-14, 16, and 18-30 were rejected under 35 USC §103(a) as unpatentable over either Henry et al. or Rawlow et al., in view of Davis et al., CNS Drugs (abstract).

These rejections of the elected pending claims are hereby traversed, in light of amendments of claims 1 and 26 herein, and the ensuing remarks. Amended claim 1 hereof recites:

1 (currently amended) A method of combating movement disorder in a patient experiencing or susceptible to same, by administering to the patient an effective amount of a neurotransmission modulating composition comprising a 5HT antagonist and/or α_2 antagonist, with the proviso that the neurotransmission modulating composition does not comprise yohimbine, cyproheptadine, or 5-MDOT.

Amended claim 26 correspondingly recites:

26. (currently amended) A method of combating movement disorder in a patient experiencing or susceptible to same, comprising administering to the patient an effective amount of a serotonergic antagonist for at least one receptor selected from the group consisting of 5HT and α_2 receptors, with the proviso that the serotonergic antagonist does not comprise yohimbine, cyproheptadine, or 5-MDOT.

All of the remaining elected pending claims are variously dependent from one of these amended claims 1 and 26.

The applicants claims thus exclude the species taught by the cited references, and there is no derivative basis in the references for applicants' invention as now claimed.

Accordingly, 1-4, 6-12, 26, 27 and 30 are patentably distinguished over Henry et al., and claims 1-4, 7, 13, 16, 26 and 27 are patentably distinguished over Rawlow, et al.

In connection with the foregoing, it is further pointed out that the Henry reference is of a speculative and tentative character, based on a rat model of Parkinson's disease acutely challenged with dopamine-replacing drugs to elicit a rotational response in 6-OHDA-lesioned rats. The reference states that:

> **"[W]hile these rats do not exhibit symptoms of dyskinesia per se, this rodent model does exhibit behaviors, the underlying mechanism of which is likely to be similar to that underlying L-DOPA-induced dyskinesia and may prove useful in studying the mol. and cellular mechanisms of L-DOPA-induced dyskinesia in Parkinson's disease." (emphasis added)**

In the rejection of claims based on Henry et al. or Rawlow et al., in view of Davis et al., Davis et al. has been cited as teaching dual α2 antagonist and 5-HT antagonist character.

On such basis, the Examiner has contended that:

> **"One skilled in the art would have been motivated to administer mirtazapine for use in methods of combating movement disorder. Such indication would have been obvious in the absence of evidence to the contrary because compounds that demonstrate 5-HT antagonism and/or α2**

antagonism are established in the prior art as effective in combating movement disorders. The determination of optimal dosages of mirtazapine as a parameter is well within the purview of those skilled in the art through no more than routine experimentation."

Davis et al. contains no teaching or suggestion of any application to movement disorder. Such reference merely states that mirtazapine is a tetracyclic anti-depressant, which is described solely as a "promising addition to currently available options for the treatment of depression." There is no teaching or suggestion of using mirtazapine as a movement disorder treatment drug.

Contrariwise, one would on the face of the Davis et al. reference avoid mirtazapine as a candidate for treatment of movement disorder, since the reference teaches that in some instances "mirtazapine, in common with many anti-depressants, was associated with potentially serious changes in haematological parameters (e.g. agranulocytosis and neutropenia). Agranulocytosis is a condition characterized by abnormally low levels of white blood cells, which compromise infection-fighting capability and can be a side effect of anti-psychotic and behavior-altering drugs. Behavioral modification drugs frequently have side effects that can include tardive dyskinesisa. Further, the reference states that clinical tolerability data suggests that mirtazapine produces fewer anticholinergic-related adverse events than tricyclic anti-depressants. These statements indicate that mirtazapine has a side effect profile that may include such adverse events, although fewer than the trycyclic anti-depressants. Anticholinergic effects include blurred vision and cognitive impairment, associated with the blockade of acetylcholine receptors.

In view of such acknowledged side effects, which on their face would appear to hold significant potential for worsening the effects of movement disorders, it is unlikely that one would be motivated to administer mirtazapine for movement disorder treatment.

Accordingly, no derivative basis for applicant's claimed invention is apparent in Davis, taken with either of the Henry et al. or Rawlow et al. references.

The Examiner contends that determination of optimal dosages of mirtazapine is a parameter well within the purview of those skilled in the art through no more than routine experimentation. This, however, overlooks the fact that the prior art in no way contemplates use of mirtazapine for treatment of movement disorder, and therefore contains no express, implied or extrapolative basis for determining any dosage for such unknown treatment.

Further, each of the Henry et al. and Rawlow et al. references fails to disclose compounds with dual α2/5HT antagonism. In the absence of any such dual activity teaching, there is further absence of motivational basis in the prior art for the hypothesized combination of teachings.

In sum, the "substantial evidence" standard required for obviousness is absent from the cited combination of references.

Based on all the foregoing, the Examiner is requested to allow claims 1-14, 16, and 18-30.

Request for Extension of Time under 37 CFR §1.136

Request hereby is made for one month extension of time, extending the time for response to the July 1, 2003 Office Action from October 1, 2003 to November 3, 2003.

The amount of $55.00 as the fee specified in 37 CFR §1.17(a) and the amount of the terminal disclaimer fee of $55.00, for a total of $110.00 is authorized to be charged in the attached credit

card authorization form. Authorization is also hereby given to charge any deficiency for this response, in applicable fees or charges, to Deposit Account Number 08-3284 of Intellectual Property/Technology Law.

Conclusion

Claims 1-14, 16, and 18-30 have been shown to be patentably distinguished over the art and are in form and condition for allowance. Favorable action is requested.

Respectfully submitted,

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